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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/625,804

07/23/2003

Subhashis Banerjee

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ABBOTT BIORESEARCH

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WORCESTER, MA 01605-4314

EXAMINER

DIBRINO, MARIANNE NMN

ART UNIT

PAPER NUMBER

1644

MAIL DATE

DELIVERY MODE

08/19/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/625,804	Applicant(s) BANERJEE, SUBHASHIS	
	Examiner DiBrino Marianne	Art Unit 1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 11 June 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-20 is/are pending in the application.
- 4a) Of the above claim(s) 8-20 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-7 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 6/11/08 has been entered.

Applicant's response filed 6/11/08 is acknowledged and has been entered.

2. Applicant is reminded of Applicant's election with traverse of Group I, a method for detecting a deantigenized Class I MHC T cell epitope, and species of dissociation constant of about 5×10^{-3} M for the binding of the deantigenized T cell epitope to soluble MHC molecule in Applicant's response filed 6/19/06.

Claims 1, 2 and 5-7 read upon the elected species.

Applicant is reminded that upon consideration of the prior art, the search had been extended to include the species of dissociation constant recited in instant claims 3 and 4.

Claims 8-20 (non-elected groups II-LXX) remain withdrawn from further consideration by the Examiner, 37 CFR 1.142(b), as being drawn to non-elected inventions.

Claims 1-7 are currently being examined

3. Applicant is reminded that the incorporation of *essential* material in the specification by reference to an unpublished U.S. application, foreign application or patent, or to a publication is improper. Applicant is required to amend the disclosure to include the material incorporated by reference, if the material is relied upon to overcome any objection, rejection, or other requirement imposed by the Office. The amendment must be accompanied by a statement executed by the applicant, or a practitioner representing the applicant, stating that the material being inserted is the material previously incorporated by reference and that the amendment contains no new matter. 37 CFR 1.57(f).

The attempt to incorporate subject matter into the instant application by reference to foreign patents and non-patent publications may be improper because an application as filed must be complete in itself in order to comply with 35 USC 112.

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An application for a patent when filed may incorporate "essential material" by reference to (1) a US patent or (2) a US patent application publication, which patent or patent publication does not itself incorporate such essential material by reference. "Essential material" is defined as that which is necessary to (1) provide a written description of the claimed invention, and the manner and process of making and using it, in such full, concise and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and set forth the best mode contemplated by the inventor of carrying out the invention, (2) describe the claimed invention in terms that particularly point out and distinctly claim the invention as required by the second paragraph of 35 USC 112, or (3) describe the structure, material or acts that correspond to a claimed means or step for performing a specified function as required by the sixth paragraph of 35 USC 112. In any application which is to issue as a US patent, essential material may not be incorporated by reference to (1) patents or applications published by foreign countries or a regional patent office, (2) non-patent publications, (3) a US patent or application which itself incorporates "essential material" by reference, or (4) a foreign application. See *In re Fouché*, 439 F.2d 1237, 169 USPQ 429 (CCPA 1971).

Nonessential subject matter may be incorporated by reference to (1) patents or applications published by the US or foreign countries or regional patent offices, (2) prior and concurrently filed, commonly owned US applications, or (3) non-patent publications. Nonessential subject matter is subject matter referred to for purposes of indicating the background of the invention or illustrating the state of the art.

Applicant is invited to determine whether material incorporated by reference is essential or non-essential and amend the specification accordingly. (See MPEP 608.01(p)).

The Examiner notes Applicant's request (page 5 of the amendment filed 6/11/08) to hold this requirement in abeyance.

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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5. Claims 1-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 00/34317 A2 (Applicant's IDS reference) and further in view of US 20050063983 A1 (of record).

Claims 1-7 have been previously rejected upon the basis set forth below.

WO 00/34317 A2 teaches reducing or eliminating a potential T cell epitope peptide's ability to bind to an MHC molecule, said MHC molecule being a class I molecule. WO 00/34317 A2 further teaches reducing or eliminating the immune response to said protein whereby one or more MHC binding peptides which are also found in the autologous organism's endogenous proteins are modified to reduce or eliminate binding to MHC molecules, while making certain that the original biological activity of the altered protein is retained. WO 00/34317 A2 teaches that the method comprises determining the amino acid sequence of the protein or the part thereof that is to be modified, identifying potential T cell epitopes within the amino acid sequence of the protein by any method including determination of the binding of peptide/MHC complexes to TCRs or T cells or analyzing the primary sequence of a protein for the presence of MHC class I binding motifs, then altering the protein or portion thereof to remove one or more of the potential T cell epitopes by alteration of one or more amino acid residues within the MHC binding peptides so that they may have reduced binding or no binding at all to an MHC molecule (especially page 4 at lines 11-26, page 7 at lines 4-19, paragraph spanning pages 8-9, page 10 at lines 11-30, page 11, page 12 at lines 1-12, page 22 at lines 4-7, examples, claims 1, 4, 14 and 15).

WO 00/34317 A2 does not teach how the one or more altered T cell epitopes are detected as recited in base claim 1 (*i.e.*, wherein said detected altered T cell epitope identifies a deantigenized T cell epitope having a binding affinity to said soluble MHC molecule less than the binding affinity of the T cell epitope to said soluble MHC molecule as recited in instant base claim 1), possessing a dissociation constant that is recited in instant claims 3-5, nor does it teach further altering an identified deantigenized T cell epitope.

US 20050063983 A1 discloses that for a peptide epitope to be useful for binding to an MHC class I molecule, it has a dissociation constant of binding of less than about 500 nM. US 20050063983 A1 further discloses identifying epitope peptides, making peptide analogs and testing such peptides for binding to purified and soluble HLA class I molecules and measuring affinity of binding (see entire reference, especially [0055], [0074], [0184], [0204] and claim 1).

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It would have been prima facie obvious to one of ordinary skill at the time the invention was made to have selected a peptide analog such as taught by WO 00/34317 A2 having a dissociation constant higher than the 500 nM value disclosed to be useful for peptide binding to MHC class I by U.S. 2050063983 A1, *i.e.*, a dissociation constant greater than 500 nM recited in instant claim 5, and including those constants recited in instant claims 3 and 4, and to have measured the binding using a soluble MHC/peptide binding assay as disclosed by U.S. 2050063983 A1.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to produce a deantigenized T cell epitope and polypeptide comprising said deantigenized T cell epitope such as taught by WO 00/34317 A2 that does not possess stable binding to an MHC class I molecule and would therefore not be useful for eliciting a T cell response because US 20050063983 A1 discloses that useful peptide binding to MHC class I occurs with a dissociation constant of less than 500 nM, WO 00/34317 A2 teaches measuring peptide binding to class I MHC, but does not disclose an assay to do so, and US 20050063983 A1 discloses a soluble MHC/peptide binding assay.

Applicant's arguments have been fully considered, but are not persuasive.

Applicant's said argument is of record on pages 5-8 of the amendment filed 6/11/08.

In arguing that neither the primary reference nor the secondary reference teach or suggest Applicant's method, Applicant is arguing the references separately. In response to Applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Applicant argues that the primary reference WO 00/34317 A2 teaches that a typical protocol within the method comprises the steps including testing of the protein or parts thereof using transgenic animals with the MHC molecules of the species to receive the therapeutic protein and altering the protein to remove one or more of the potential T cells epitopes. Applicant further argues that said primary reference does not teach providing an amino acid sequence of a T cell epitope having a binding affinity to a soluble MHC molecule, contacting the altered T cell epitope with a soluble MHC molecule, wherein the said altered epitope has a binding affinity to the soluble MHC molecule less than the binding affinity of the T cell epitope to the soluble MHC molecule. Applicant asserts that for the first time described herein is a method for detecting a deantigenized T cell epitope, which method employs a cell solubilized or genetically produced MHC molecule, *i.e.*, soluble MHC, for peptide screening and binding assays, although such assays have been described for detecting peptides that induce or increase CTL responses as compared to a parental peptide.

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The method recited in instant base claim 1 recites "said method comprising" the recited steps. The primary reference WO 00/34317 A2 teaches a method that comprises identifying potential T cell epitopes within the amino acid sequence of a protein by any method, including determination of the binding of peptides to MHC molecules determining binding of peptide/MHC complexes to TCRs, testing the protein or peptide parts thereof using transgenic animals with the MHC molecules of the species to receive the therapeutic protein, *i.e.*, the step that correlates with the providing an amino acid sequence of a T cell epitope step of instant base claim 1 teaches that such providing (*i.e.*, identifying a T cell epitope) may be accomplished through an *in vitro* binding assay. The said primary reference further teaches that having identified potential T cell epitopes, these epitopes are "eliminated" by alteration of one or more amino acids within the epitope itself, including by substitution of an MHC binding motif amino acid residue(s). Although the primary reference does not teach a soluble, MHC/peptide binding assay, the secondary reference provides such teaching. With regard to the use of a soluble MHC/peptide binding assay to detect peptides that bind with lower affinity to an MHC molecule, one of ordinary skill in the art at the time the invention was made would have been aware that an assay to detect binding and/or affinity of binding could be used to measure said binding and/or affinity over a range of affinities, high and low.

6. Claims 1-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 2002/0119492 A1 (of record) and further in view of DiBrino *et al* (J. Immunol. 1993, 151(11): 5930-5935, of record) and US 20050063983 A1 (of record).

Claims 1-7 have been previously rejected upon the basis set forth below.

US 2002/0119492 A1 discloses a method for generating a modified polypeptide that exhibits reduced immunogenicity wherein a T cell epitope(s) is identified that binds to a class I MHC molecule, said method including computational methods or physical methods such as high affinity binding assays, the epitope(s) is altered to reduce or eliminate binding to said class I MHC molecule, and the modified polypeptide is tested to insure that its activity is similar to its activity before it was modified (especially abstract, [0016], [0029], [0032], [0039], [0040], [0123]-[0127] [0132], [0135], [0139], [0142], [0146]-[0148], claims).

US 2002/0119492 A1 does not disclose wherein the altered T cell epitope is evaluated by contacting the altered T cell epitope with a soluble MHC class I molecule for sufficient time to permit MHC-epitope binding complexes to form, nor does it disclose a step to measure the dissociation constant of the said altered T cell epitope.

DiBrino *et al* teach that the presence of anchor residues is not sufficient for binding to a class I MHC molecule, some amino acid residues other than the most favorable anchor residues can be accommodated for peptide binding, and amino acid residues at other positions may be important for binding (especially last two paragraphs of article).

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DiBrino *et al* further teach a peptide binding assay using soluble MHC class I molecules that measures the stability of HLA complexes by measuring the rate of dissociation of iodinated β 2m at 37 degrees C (especially materials and methods section at column 2, paragraph 1).

US 20050063983 A1 discloses that for a peptide epitope to be useful for binding to an MHC class I molecule, it has a dissociation constant of binding of less than about 500 nM. US 20050063983 A1 further discloses identifying epitope peptides, making peptide analogs and testing such peptides for binding to purified and soluble HLA class I molecules and measuring affinity of binding (see entire reference, especially [0055], [0074], [0184], [0204] and claim 1).

It would have been *prima facie* obvious to one of ordinary skill at the time the invention was made to have identified potential T cell epitope peptide(s) in a polypeptide as disclosed by US 2002/0119492 A1, to have tested the peptide(s) for reduced or no ability to bind to a selected MHC class I molecule using an assay as taught by DiBrino *et al*, to have selected a peptide(s) having a dissociation constant higher than the value disclosed to be useful for peptide binding to MHC class I by US 20050063983 A1, *i.e.*, a dissociation constant greater than 500 nM recited in instant claim 5 and including those constants recited in instant claims 3 and 4, and to have constructed an altered less immunogenic polypeptide with similar biological activity to the unaltered polypeptide as disclosed by US 2002/0119492 A1.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to produce a deantigenized T cell epitope(s) and protein containing said epitope(s) such as taught by US 2002/0119492 A1, said epitope does not possess stable binding to an MHC class I molecule and would therefore not be useful for eliciting a T cell response because US 20050063983 A1 discloses that useful peptide binding to MHC class I occurs with a dissociation constant less than 500 nM, and DiBrino *et al* teach that the presence, or by extension, absence of anchor residues does not always correlate with peptide binding or altered binding when potential MHC class I binding peptides are identified on the basis of their anchor amino acid residues, and DiBrino *et al* teach an assay for measuring the binding of said peptides to a selected soluble MHC class I molecule.

Claim 2 is included in this rejection because the art reference teaches providing one or more altered T cell epitopes that are different. The Examiner notes that the claim language does not recite that the deantigenized T cell epitope is improved upon by further altering its sequence.

Applicant's arguments have been fully considered, but are not persuasive.

Applicant's said argument is of record on pages 5-8 of the amendment filed 6/11/08.

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In arguing that neither the primary reference nor the secondary reference teach or suggest Applicant's method, Applicant is arguing the references separately. In response to Applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Applicant also argues that the Examiner has used hindsight reasoning. In response to Applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the Applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

With regard to Applicant's argument that DiBrino *et al* do not teach or suggest the use of a soluble MHC assay to detect modified T cell epitopes having reduced or no immunogenicity, of ordinary skill in the art at the time the invention was made would have been aware that such assay could be used to measure binding of peptides having a wide range of affinities, from high to low.

In response to Applicant's argument that there is no suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art to modify the references or to combine the reference teaching to arrive at the claimed invention, one of ordinary skill in the art at the time the invention was made would have been motivated to combine the references with a reasonable expectation of success in producing the claimed invention because US 2002/0119492 A1 discloses identifying a T cell epitope(s) that binds to a class I MHC molecule using computational methods or a physical method such as a high affinity binding assay, and altering the epitopes(s) to reduce or eliminate binding to the class I molecule, but does not teach what the actual binding assays are that are used to identify and test the epitope(s) and the altered epitope(s), DiBrino *et al* teach a peptide binding assay using soluble MHC class I molecules and that it is important to test the actual binding of peptides having anchor residues because the presence of anchor residues (or by extension, the use of computational methods that rely on the presence of anchor residues) is not sufficient for binding to a MHC class I molecule, and US 20050063983 A1 discloses that for a peptide epitope to be useful for binding to an MHC class I molecule, it must have a dissociation constant of binding of less than about 500 nM, and by extension, one that is a weak binder or doesn't bind has a dissociation constant higher than about 500 nM.

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7. Claims 1-7 stand rejected under 35 U.S.C. 103(a) as being unpatentable over US 2002/0119492 A1 (of record) in view of DiBrino *et al* (J. Immunol. 1993, 151(11): 5930-5935, of record).

US 2002/0119492 A1 discloses a method for generating a modified polypeptide that exhibits reduced immunogenicity wherein a T cell epitope(s) is identified that binds to a class I MHC molecule, said method including computational methods or physical methods such as high affinity binding assays, the epitope(s) is altered to reduce or eliminate binding to said class I MHC molecule, and the modified polypeptide is tested to insure that its activity is similar to its activity before it was modified (especially abstract, [0016], [0029], [0032], [0039], [0040], [0123]-[0127] [0132], [0135], [0139], [0142], [0146]-[0148], claims).

US 2002/0119492 A1 does not disclose wherein the altered T cell epitope is evaluated by contacting the altered T cell epitope with a soluble MHC class I molecule for sufficient time to permit MHC-epitope binding complexes to form.

DiBrino *et al* teach that the presence of anchor residues is not sufficient for binding to a class I MHC molecule, some amino acid residues other than the most favorable anchor residues can be accommodated for peptide binding, and amino acid residues at other positions may be important for binding (especially last two paragraphs of article). DiBrino *et al* further teach a peptide binding assay using soluble MHC class I molecules that measures the stability of HLA complexes by measuring the rate of dissociation of iodinated $\beta 2m$ at 37 degrees C (especially materials and methods section at column 2, paragraph 1).

It would have been prima facie obvious to one of ordinary skill at the time the invention was made to have identified potential T cell epitope peptide(s) in a polypeptide as disclosed by US 2002/0119492 A1, to have tested the peptide(s) for reduced or no ability to bind to a selected MHC class I molecule using an assay as taught by DiBrino *et al*, and to have constructed an altered less immunogenic polypeptide with similar biological activity to the unaltered polypeptide as disclosed by US 2002/0119492 A1.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to produce a deantigenized T cell epitope(s) and altered polypeptide containing said epitope(s) such as taught by US 2002/0119492 A1 that does not possess stable binding to an MHC class I molecule and would therefore not be useful for eliciting a T cell response because DiBrino *et al* teach that the presence, or by extension, absence of anchor residues does not always correlate with peptide binding or altered binding when potential MHC class I binding peptides are identified on the basis of their anchor amino acid residues, and DiBrino *et al* teach an assay for measuring the binding of said peptides to a selected soluble MHC class I molecule.

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Claim 2 is included in this rejection because the art reference teaches providing one or more altered T cell epitopes that are different. The Examiner notes that the claim language does not recite that the deantigenized T cell epitope is improved upon by further altering its sequence.

The Examiner notes that there is no recitation of a method step in the instant claims to test or produce a deantigenized T cell epitope having the said dissociation constant, the identified deantigenized T cell epitope merely possesses the property of having the recited dissociation constant. In addition it is an expected property of a T cell epitope that is altered to eliminate its ability to bind MHC class I that it would possess a dissociation a dissociation constant greater than 500 nM recited in instant claim 5, and including those constants recited in instant claims 3 and 4.

Applicant's arguments have been fully considered, but are not persuasive.

Applicant's said argument is of record on pages 5-8 of the amendment filed 6/11/08 (same argument as presented for the rejection immediately supra).

The Examiner's response to Applicant's arguments supra at item #6 of this Office Action as pertains to US 2002/0119492 A1 and DiBrino *et al* apply herein.

Applicant is arguing the references separately. Furthermore, one of ordinary skill in the art at the time the invention was made would have been motivated to combine the references with a reasonable expectation of success in producing the claimed invention because US 2002/0119492 A1 discloses identifying a T cell epitope(s) that binds to a class I MHC molecule using computational methods or a physical method such as a high affinity binding assay, and altering the epitopes(s) to reduce or eliminate binding to the class I molecule, but does not teach what binding assays are used to identify and test the epitope(s) and the altered epitope(s), and DiBrino *et al* teach a peptide binding assay using soluble MHC class I molecules and that it is important to test the binding of peptides having anchor residues because the presence of anchor residues (or by extension, the use of computational methods that rely on the presence of anchor residues) is not sufficient for binding to a MHC class I molecule.

8. No claim is allowed.

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9. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Marianne DiBrino whose telephone number is 571-272-0842. The Examiner can normally be reached on Monday, Tuesday, Thursday and Friday.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Eileen B. O'Hara, can be reached on 571-272-0878. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Marianne DiBrino, Ph.D.
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August 7, 2008

/G.R. Ewoldt/
Primary Examiner, Art Unit 1644